Current Status of the Claims:

This listing of claims will replace the listing of claims in the application:

Listing of Claims:

1. (Original) An isolated infectious chimeric respiratory syncytial virus (RSV) comprising a major nucleocapsid (N) protein, a nucleocapsid phosphoprotein (P), a large polymerase protein (L), a RNA polymerase elongation factor, and a partial or complete RSV background genome or antigenome of a human or bovine RSV combined with one or more heterologous gene(s) and/or genome segment(s) of a different RSV to form a human-bovine chimeric RSV genome or antigenome.

2. (Original) The chimeric RSV of claim 1, wherein said one or more heterologous gene(s) and/or genome segment(s) include one or more RSV NS1, NS2, N, P, M, SH, M2(ORF1), M2(ORF2), L, F or G gene(s) or genome segment(s) or a leader, trailer or intergenic region of the RSV genome or a segment thereof.

3. (Original) The chimeric RSV of claim 2, wherein said one or more heterologous gene(s) and/or genome segment(s) includes one or more gene(s) or genome segment(s) encoding a RSV F, G and/or SH glycoprotein or an immunogenic domain or epitope thereof.

4. (Original) The chimeric RSV of claim 1, wherein the human-bovine chimeric RSV genome or antigenome encodes a chimeric glycoprotein having both human and bovine glycoprotein domains or immunogenic epitopes.

5. (Original) The chimeric RSV of claim 4, wherein said one or more heterologous gene(s) and/or genome segment(s) includes a gene segment encoding a glycoprotein ectodomain.

6. (Original) The chimeric RSV of claim 1, wherein a heterologous gene or genome segment is substituted for a counterpart gene or genome segment in a partial RSV background genome or antigenome.

7. (Original) The chimeric RSV of claim 1, wherein a heterologous gene or genome segment is added adjacent to, within, or as a replacement to, a noncoding region of the partial or complete RSV background genome or antigenome.

8. (Original) The chimeric RSV of claim 1, wherein a heterologous gene or genome segment is added or substituted at a position corresponding to a wild-type gene order position of a counterpart gene or genome segment within the partial or complete RSV background genome or antigenome.

9. (Original) The chimeric RSV of claim 1, wherein a heterologous gene or genome segment is added or substituted at a position that is more promoter-proximal or promoter-distal compared to a wild-type gene order position of a counterpart gene or genome segment within the partial or complete RSV background genome or antigenome.

10. (Original) The chimeric RSV of claim 1, wherein the chimeric genome or antigenome comprises a partial or complete human RSV background genome or antigenome combined with one or more heterologous gene(s) and/or genome segment(s) from a bovine RSV.

11. (Original) The chimeric RSV of claim 10, wherein one or more genes selected from N, P, NS1, NS2, M2-1 and M of a human RSV is/are replaced by one or more heterologous gene(s) from a bovine RSV.

12. (Original) The chimeric RSV of claim 11, wherein both N and P genes of a human RSV are replaced by counterpart N and P genes from a bovine RSV.

13. (Original) The chimeric RSV of claim 11, wherein both NS1 and NS2 genes of a human RSV are replaced by counterpart NS1 and NS2 genes from a bovine RSV.

14. (Original) The chimeric RSV of claim 11, wherein two or more of the M2-1, M2-2 and L genes are replaced by counterpart genes from a bovine RSV

15. (Original) The chimeric RSV of claim 11, wherein each of the N, P, NS1, NS2, M2-1 and M genes of a human RSV are replaced by counterpart N, P, NS1, NS2, M2-1 and M genes from a bovine RSV.

16. (Original) The chimeric RSV of claim 1, wherein the chimeric genome or antigenome comprises a partial or complete bovine RSV background genome or antigenome combined with one or more heterologous gene(s) and/or genome segment(s) from a human RSV.

17. (Original) The chimeric RSV of claim 16, wherein one or more human RSV glycoprotein genes selected from F, G and SH, or one or more genome segment(s) encoding cytoplasmic domain, transmembrane domain, ectodomain or immunogenic epitope portion(s) of F, G, and/or SH is/are added or substituted within a partial or complete bovine RSV background genome or antigenome.

18. (Original) The chimeric RSV of claim 17, wherein one or both human RSV glycoprotein genes F and G is/are substituted to replace one or both counterpart F and G glycoprotein genes in a partial bovine RSV background genome or antigenome.

19. (Original) The chimeric RSV of claim 17, wherein the human-bovine chimeric genome or antigenome incorporates antigenic determinants from one or both subgroup A and subgroup B human RSV.

20. (Original) The chimeric RSV of claim 17, wherein both human RSV glycoprotein genes F and G are substituted to replace counterpart F and G glycoprotein genes in the bovine RSV background genome or antigenome.

21. (Original) The chimeric RSV of claim 20, which is rBRSV/A2.

22. (Original) The chimeric RSV of claim 9, wherein one or more human RSV glycoprotein genes selected from F, G and SH is/are added or substituted at a position that is more promoter-proximal compared to a wild-type gene order position of a counterpart gene or genome segment within a partial or complete bovine RSV background genome or antigenome.

23. (Original) The chimeric RSV of claim 22, wherein both human RSV glycoprotein genes G and F are substituted at gene order positions 1 and 2, respectively, to replace counterpart G and F glycoprotein genes deleted at wild type positions 7 and 8, respectively in a partial bovine RSV background genome or antigenome.

24. (Original) The chimeric RSV of claim 23, which is rBRSV/A2-G1F2

25. (Original) The chimeric RSV of claim 17, wherein the chimeric genome or antigenome is further modified by addition or substitution of one or more additional heterologous gene(s) or genome segment(s) from a human RSV within the partial or complete

bovine background genome or antigenome to increase genetic stability or alter attenuation, reactogenicity or growth in culture of the chimeric virus.

26. (Original) The chimeric RSV of claim 16, wherein one or more human RSV envelope-associated genes selected from F, G, SH, and M is/are added or substituted within a partial or complete bovine RSV background genome or antigenome.

27. (Original) The chimeric RSV of claim 26, wherein one or more human RSV envelope-associated genes selected from F, G, SH, and M is/are added or substituted within a partial bovine RSV background genome or antigenome in which one or more envelope-associated genes selected from F, G, SH, and M is/are deleted.

28. (Original) The chimeric RSV of claim 27, wherein human RSV envelope-associated genes F, G, and M are added within a partial bovine RSV background genome or antigenome in which envelope-associated genes F, G, SH, and M are deleted.

29. (Original) The chimeric RSV of claim 28, which is rBRSV/A2-MGF.

30. (Original) The chimeric RSV of claim 1, wherein the chimeric genome or antigenome incorporates at least one and up to a full complement of attenuating mutations present within a panel of mutant human RSV strains, said panel comprising cpts RSV 248 (ATCC VR 2450), cpts RSV 248/404 (ATCC VR 2454), cpts RSV 248/955 (ATCC VR 2453), cpts RSV 530 (ATCC VR 2452), cpts RSV 530/1009 (ATCC VR 2451), cpts RSV 530/1030 (ATCC VR 2455), RSV B-1 cp52/2B5 (ATCC VR 2542), and RSV B-1 cp-23 (ATCC VR 2579).

31. (Original) The chimeric RSV of claim 30, wherein the chimeric genome or antigenome incorporates attenuating mutations adopted from different mutant RSV strains.

32. (Original) The chimeric RSV of claim 1, wherein the chimeric genome or antigenome incorporates at least one and up to a full complement of attenuating mutations specifying an amino acid substitution at Val267 in the RSV N gene, Glu218 and/or Thr523 in the RSV F gene, Asn43, Cys319, Phe 521, Gln831, Met1169, Tyr1321 and/or His 1690 in the RSV polymerase gene L, and a nucleotide substitution in the gene-start sequence of gene M2.

33. (Original) The chimeric RSV of claim 32, wherein the chimeric genome or antigenome incorporates at least two attenuating mutations.

34. (Original) The chimeric RSV of claim 32, wherein the chimeric genome or antigenome includes at least one attenuating mutation stabilized by multiple nucleotide changes in a codon specifying the mutation.

35. (Original) The chimeric RSV of claim 1, wherein the chimeric genome or antigenome further comprises a nucleotide modification specifying a phenotypic change selected from a change in growth characteristics, attenuation, temperature-sensitivity, cold-adaptation, plaque size, host-range restriction, or a change in immunogenicity.

36. (Original) The chimeric RSV of claim 35, wherein the nucleotide modification alters a SH, NS1, NS2, M2ORF2, or G gene of the chimeric virus.

37. (Original) The chimeric RSV of claim 36, wherein a SH, NS1, NS2, M2 ORF2, or G gene of the chimeric virus is deleted in whole or in part or expression of the gene is ablated by introduction of one or more stop codons in an open reading frame of the gene.

38. (Original) The chimeric RSV of claim 35, wherein the nucleotide modification comprises a nucleotide deletion, insertion, substitution, addition or rearrangement of a cis-acting regulatory sequence of a selected gene within the chimeric RSV genome or antigenome.

39. (Original) The chimeric RSV of claim 38, wherein a gene end (GE) signal of the NS1 or NS2 gene is modified.

40. (Original) The chimeric RSV of claim 35, wherein the nucleotide modification comprises an insertion, deletion, substitution, or rearrangement of a translational start site within the chimeric genome or antigenome.

41. (Original) The chimeric RSV of claim 40, wherein the translational start site for a secreted form of the RSV G glycoprotein is ablated.

42. (Original) The chimeric RSV of claim 35, wherein the chimeric genome or antigenome is modified to encode a non-RSV molecule selected from a cytokine, a T-helper

epitope, a restriction site marker, or a protein of a microbial pathogen capable of eliciting a protective immune response in a mammalian host.

43. (Original) The chimeric RSV of claim 35, which incorporates one or more gene(s) and/or genome segment(s) from parainfluenza virus (PIV).

44. (Original) The chimeric RSV of claim 43, wherein the chimeric genome or antigenome encodes a PIV HN or F glycoprotein or immunogenic domain or epitope thereof.

45. (Original) The chimeric RSV of claim 44, wherein the chimeric genome or antigenome encodes an ectodomain or immunogenic epitope of HN or F of PIV1, PIV2, or PIV3.

46. (Original) The chimeric RSV of claim 1 which is a virus.

47. (Original) The chimeric RSV of claim 1 which is a subviral particle.

48. (Original) A method for stimulating the immune system of an individual to induce protection against RSV which comprises administering to the individual an immunologically sufficient amount of the chimeric RSV of claim 1 combined with a physiologically acceptable carrier.

49. (Original) The method of claim 48, wherein the chimeric RSV is administered in a dose of 10^3 to 10^6 PFU.

50. (Original) The method of claim 48, wherein the chimeric RSV is administered to the upper respiratory tract.

51. (Original) The method of claim 48, wherein the chimeric RSV is administered by spray, droplet or aerosol.

52. (Original) The method of claim 48, wherein the chimeric RSV is administered to an individual seronegative for antibodies to RSV or possessing transplacentally acquired maternal antibodies to RSV.

53. (Original) The method of claim 48, wherein the chimeric RSV elicits an immune response against either human RSV A or RSV B.

54. (Original) The method of claim 48, wherein the chimeric RSV elicits an immune response against both human RSV A and RSV B.

55. (Original) The method of claim 48, wherein the chimeric RSV elicits an immune response against either human RSV A or RSV B and is co-administered with an immunologically sufficient amount of a second attenuated RSV capable of eliciting an immune response against human RSV A or RSV B, whereby an immune response is elicited against both human RSV A and RSV B.

56. (Original) The method of claim 55, wherein the chimeric RSV and second attenuated RSV are administered simultaneously as a mixture.

57. (Original) An immunogenic composition to elicit an immune response against RSV comprising an immunologically sufficient amount of the chimeric RSV of claim 1 in a physiologically acceptable carrier.

58. (Original) The immunogenic composition of claim 57, formulated in a dose of 10^3 to 10^6 PFU.

59. (Original) The immunogenic composition of claim 57, formulated for administration to the upper respiratory tract by spray, droplet or aerosol.

60. (Original) The immunogenic composition of claim57, wherein the chimeric RSV elicits an immune response against either human RSV A or RSV B.

61. (Original) The immunogenic composition of claim 57, wherein the chimeric RSV elicits an immune response against both human RSV A and RSV B

62. (Original) The immunogenic composition of claim 57, wherein the chimeric RSV elicits an immune response against either human RSV A or RSV B and wherein the composition further comprises an immunologically sufficient amount of a second attenuated RSV capable of eliciting an immune response against human RSV A or RSV B, whereby the composition elicits an immune response against both human RSV A and RSV B.

63. (Withdrawn) An isolated polynucleotide molecule comprising a chimeric RSV genome or antigenome which includes a partial or complete RSV background genome or antigenome of a human or bovine RSV combined with one or more heterologous gene(s) or genome segment(s) of a different RSV to form a human-bovine chimeric RSV genome or antigenome.

64. (Withdrawn) The isolated polynucleotide of claim 63, wherein said one or more heterologous gene(s) and/or genome segment(s) include one or more RSV NS1, NS2, N, P, M, SH, M2(ORF1), M2(ORF2), L, F or G gene(s) or genome segment(s) or a leader, trailer or intergenic region of the RSV genome or a segment thereof.

65. (Withdrawn) The isolated polynucleotide of claim 63, wherein a heterologous gene or genome segment is substituted for a counterpart gene or genome segment in a partial RSV background genome or antigenome.

66. (Withdrawn) The isolated polynucleotide of claim 63, wherein a heterologous gene or genome segment is added adjacent to, within, or as a replacement to, a noncoding region of the partial or complete RSV background genome or antigenome.

67. (Withdrawn) The isolated polynucleotide of claim 63, wherein a heterologous gene or genome segment is added or substituted at a position that is more promoter-proximal or promoter-distal compared to a wild-type gene order position of a counterpart gene or genome segment within the partial or complete RSV background genome or antigenome.

68. (Withdrawn) The isolated polynucleotide of claim 63, wherein the chimeric genome or antigenome comprises a partial or complete human RSV background genome or antigenome combined with one or more heterologous gene(s) and/or genome segment(s) from a bovine RSV.

69. (Withdrawn) The isolated polynucleotide of claim 68, wherein one or more genes selected from N, P, NS1, NS2, M2-1 and M of a human RSV is/are replaced by one or more heterologous gene(s) from a bovine RSV.

70. (Withdrawn) The isolated polynucleotide of claim 68, wherein both N and P genes of a human RSV are replaced by counterpart N and P genes from a bovine RSV.

71. (Withdrawn) The isolated polynucleotide of claim 68, wherein both NS1 and NS2 genes of a human RSV are replaced by counterpart NS1 and NS2 genes from a bovine RSV.

72. (Withdrawn) The isolated polynucleotide of claim 68, wherein two or more of the M2-1, M2-2 and L genes are replaced by counterpart genes from a bovine RSV

73. (Withdrawn) The isolated polynucleotide of claim 63, wherein the chimeric genome or antigenome comprises a partial or complete bovine RSV background genome or antigenome combined with one or more heterologous gene(s) and/or genome segment(s) from a human RSV.

74. (Withdrawn) The isolated polynucleotide of claim 73, wherein one or more human RSV glycoprotein genes selected from F, G and SH, or one or more genome segment(s) encoding cytoplasmic domain, transmembrane domain, ectodomain or immunogenic epitope portion(s) of F, G, and/or SH is/are added or substituted within a partial or complete bovine RSV background genome or antigenome.

75. (Withdrawn) The isolated polynucleotide of claim 74, wherein one or both human RSV glycoprotein genes F and G is/are substituted to replace one or both counterpart F and G glycoprotein genes in a partial bovine RSV background genome or antigenome.

76. (Withdrawn) The isolated polynucleotide of claim 75, wherein both human RSV glycoprotein genes F and G are substituted to replace counterpart F and G glycoprotein genes in the bovine RSV background genome or antigenome.

77. (Withdrawn) The isolated polynucleotide of claim 67, wherein one or more human RSV glycoprotein genes selected from F, G and SH is/are added or substituted at a position that is more promoter-proximal compared to a wild-type gene order position of a counterpart gene or genome segment within a partial or complete bovine RSV background genome or antigenome.

78. (Withdrawn) The isolated polynucleotide of claim 77, wherein both human RSV glycoprotein genes G and F are substituted at gene order positions 1 and 2, respectively, to

replace counterpart G and F glycoprotein genes deleted at wild type positions 7 and 8, respectively in a partial bovine RSV background genome or antigenome.

79. (Withdrawn) The isolated polynucleotide of claim 73, wherein the chimeric genome or antigenome is further modified by addition or substitution of one or more additional heterologous gene(s) or genome segment(s) from a human RSV within the partial or complete bovine background genome or antigenome to increase genetic stability or alter attenuation, reactogenicity or growth in culture of the chimeric virus.

80. (Withdrawn) The isolated polynucleotide of claim 73, wherein one or more human RSV envelope-associated genes selected from F, G, SH, and M is/are added or substituted within a partial or complete bovine RSV background genome or antigenome.

81. (Withdrawn) The isolated polynucleotide of claim 80, wherein human RSV envelope-associated genes F, G, and M are added within a partial bovine RSV background genome or antigenome in which envelope-associated genes F, G, SH, and M are deleted.

82. (Withdrawn) The isolated polynucleotide molecule of claim 63, wherein the human-bovine chimeric genome or antigenome incorporates antigenic determinants from both subgroup A and subgroup B human RSV.

83. (Withdrawn) The isolated polynucleotide molecule of claim 63, wherein the chimeric genome or antigenome is further modified by incorporation of one or more attenuating mutations.

84. (Withdrawn) The isolated polynucleotide molecule of claim 63, further comprising a nucleotide modification specifying a phenotypic change selected from a change in growth characteristics, attenuation, temperature-sensitivity, cold-adaptation, plaque size, host-range restriction, or a change in immunogenicity.

85. (Withdrawn) The isolated polynucleotide molecule of claim 63, wherein a SH, NS1, NS2, M2ORF2, or G gene is modified.

86. (Withdrawn) The isolated polynucleotide molecule of claim 85, wherein the SH, NS1, NS2, M2 ORF2, or G gene is deleted in whole or in part or expression of the gene is ablated by introduction of one or more stop codons in an open reading frame of the gene.

87. (Withdrawn) The isolated polynucleotide molecule of claim 59, wherein the nucleotide modification comprises a nucleotide deletion, insertion, addition or rearrangement of a cis-acting regulatory sequence of a selected RSV gene within the chimeric RSV genome or antigenome.

88. (Original) A method for producing an infectious attenuated chimeric RSV particle from one or more isolated polynucleotide molecules encoding said RSV, comprising:

expressing in a cell or cell-free lysate an expression vector comprising an isolated polynucleotide comprising a partial or complete RSV background genome or antigenome of a human or bovine RSV combined with one or more heterologous gene(s) or genome segment(s) of a different RSV to form a human-bovine chimeric RSV genome or antigenome, and RSV N, P, L and RNA polymerase elongation factor proteins.

89. (Original) The method of claim 88, wherein the chimeric RSV genome or antigenome and the N, P, L and RNA polymerase elongation factor proteins are expressed by two or more different expression vectors.

90. (Original) The chimeric RSV of claim 1, wherein the bovine-human chimeric genome or antigenome comprises a partial or complete RSV vector genome or antigenome combined with one or more heterologous genes or genome segments encoding one or more antigenic determinants of one or more heterologous pathogens.

91. (Original) The chimeric RSV of claim 90, wherein said one or more heterologous pathogens is a heterologous RSV and said heterologous gene(s) or genome segment(s) encode(s) one or more RSV NS1, NS2, N, P, M, SH, M2(ORF1), M2(ORF2), L, F or G protein(s) or fragment(s) thereof.

92. (Original) The chimeric RSV of claim 90, wherein the vector genome or antigenome is a partial or complete RSV A genome or antigenome and the heterologous gene(s) or genome segment(s) encoding the antigenic determinant(s) is/are of a RSV B subgroup virus.

93. (Original) The chimeric RSV of claim 90, wherein the chimeric genome or antigenome incorporates one or more gene(s) or genome segment(s) of a BRSV that specifies attenuation.

94. (Original) The chimeric RSV of claim 90, wherein one or more HPIV1, HPIV2, or HPIV3 gene(s) or genome segment(s) encoding one or more HN and/or F glycoprotein(s) or antigenic domain(s), fragment(s) or epitope(s) thereof is/are added to or incorporated within the partial or complete HRSV vector genome or antigenome.

95. (Original) The chimeric RSV of claim 90, wherein a transcription unit comprising an open reading frame (ORF) of an HPIV2 HN or F gene is added to or incorporated within the chimeric HRSV vector genome or antigenome.

96. (Original) The chimeric RSV of claim 35, wherein the vector genome or antigenome is a partial or complete BRSV genome or antigenome and the heterologous gene(s) or genome segment(s) encoding the antigenic determinant(s) is/are of one or more HRSV(s).

97. (Original) The chimeric RSV of claim 96, wherein the partial or complete BRSV genome or antigenome incorporates one or more gene(s) or genome segment(s) encoding one or more HRSV glycoprotein genes selected from F, G and SH, or one or more genome segment(s) encoding cytoplasmic domain, transmembrane domain, ectodomain or immunogenic epitope portion(s) of F, G, and/or SH of HRSV.

98. (Original) The chimeric RSV of claim 90, wherein the vector genome or antigenome is a partial or complete HRSV or BRSV genome or antigenome and the heterologous pathogen is selected from measles virus, subgroup A and subgroup B respiratory syncytial viruses, mumps virus, human papilloma viruses, type 1 and type 2 human immunodeficiency viruses, herpes simplex viruses, cytomegalovirus, rabies virus, Epstein Barr virus, filoviruses, bunyaviruses, flaviviruses, alphaviruses and influenza viruses.

99. (Original) The chimeric RSV of claim 98, wherein said one or more heterologous antigenic determinant(s) is/are selected from measles virus HA and F proteins, subgroup A or subgroup B respiratory syncytial virus F, G, SH and M2 proteins, mumps virus HN and F proteins, human papilloma virus L1 protein, type 1 or type 2 human immunodeficiency virus gp160 protein, herpes simplex virus and cytomegalovirus gB, gC, gD, gE, gG, gH, gI, gJ, gK, gL, and gM proteins, rabies virus G protein, Epstein Barr Virus gp350 protein; filovirus G protein, bunyavirus G protein, Flavivirus E and NS1 proteins, and alphavirus E protein, and antigenic domains, fragments and epitopes thereof.

100. (Original) The chimeric RSV of claim 99, wherein the heterologous pathogen is measles virus and the heterologous antigenic determinant(s) is/are selected from the measles virus HA and F proteins and antigenic domains, fragments and epitopes thereof.

101. (Original) The chimeric RSV of claim 100, wherein a transcription unit comprising an open reading frame (ORF) of a measles virus HA gene is added to or incorporated within a HRSV vector genome or antigenome.